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|---|---|
| NGUYEN, Q | |
| **ART UNIT** | **PAPER NUMBER** |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

| Office Action Summary | Application No. 09/117,218 | Applicant(s) BROWN ET AL. | |
|---|---|---|---|
| | Examiner Quang Nguyen, Ph.D. | Art Unit 1632 | |

*-- The MAILING DATE of this communication appears on th cover sheet with the correspond nce address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

**Status**

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☒ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☒ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

**Attachment(s)**

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9 .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

## DETAILED ACTION

### *Claim Rejections - 35 USC § 101*

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-10 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966). For the purpose of compact prosecution, these claims will be treated as composition claims drawn to a mutant herpes simplex virus.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising of a mutant herpes simplex virus-1 strain 1716 comprising a 759-bp deletion in gamma 34.5 gene in treating mesothelioma and melanoma in mouse, and a method of treating mesothelioma and melanoma in mouse comprising the step of intratumoral injection of an effective

amount of the same mutant HSV-1, wherein said mutant HSV-1 infects, replicates and lyses tumor cells and thereby treating cancer in mouse, does not reasonably provide enablement for a composition comprising any and all mutant herpes simplex virus having a modified gamma 34.5 gene to treat any and all non-neuronal cancers in any and all mammal, or a method of treating any and all non-neuronal cancer in any and all mammal by delivering an effective amount of the same composition through any and all routes of administration to the mammal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in the determination of an enabling disclosure have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex parte Forman*, (230 USPQ 546 (Bd Pat. Appl & Unt, 1986); *In re Wands*, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)).

The claims are drawn to the use of a mutant herpes simplex virus which has been modified in the gamma 34.5 gene such that the gene is non-functional to treat non-neuronal cancer, an agent comprising the same mutant herpes simplex virus and a method utilizing the same mutant herpes simplex virus in treating non-neuronal cancer in a mammal.

The specification discloses various deletion and point mutants in the RL1 gene coding for the ICP 34.5 protein (or gamma 34.5 gene) for both HSV-1 strain 17 and

HSV-2 strain HG52, including, HSV-1 strains 1716, 1771 and HSV-2 strains 2604, 2616, 2621. The specification teaches that HSV-1716 mutant replicates efficiently *in vitro* in both human malignant mesothelioma cell line REN and melanoma cell line 1205. HSV-1716 mutant has also been shown to lyse REN cells and I-45 cells (another human mesothelioma cell line) effectively *in vitro*. Using a model of human malignant mesothelioma growing in the peritoneal cavity of SCID mice, and SCID mice with pre-formed intracutaneous 1205 tumors, the specification discloses that administration of HSV-1716 mutant into tumor-bearing mice resulted in a decrease in tumor mass and an improvement in survival. The specification further teaches that the HSV-1716 mutant is replication restricted to tumor cells causing oncolytic activity, and that it does not disseminate or persist in treated mice.

The above evidence is noted and considered. However, it can not be extrapolated to the instant claimed invention which is directed to a composition and a method utilizing any and all mutant HSV having a modified gamma 34.5 gene to treat any and all non-neuronal cancers (encompassing both primary and metastatic tumors) in any and all mammal, including human, through any and all routes of administering the mutant HSV to the mammal.

The specification is not enabled for such a broadly claimed invention. There are several issues that need to be addressed. With respect to a broad scope in utilizing any and all mutant herpes simplex virus having a modified gamma 34.5 gene for non-neuronal cancer treatment, the specification teaches specifically the use of HSV-1716 in reducing mesothelioma and melanoma tumor burden in mice through its oncolytic

activity and this virus strain replicates restrictedly only in tumor cells and does not disseminate or persist in treated mice. However, the specification does not provide any guidance or examples of mutant HSV strains other than HSV-1716 having the same effects in treating mesothelioma and melanoma bearing mice or other mammal. It is well known in the art that different viral strains differ in pathogenicity and many host factors such as animal age, route of administration, and animal strain have influence on the susceptibility of HSV infection. As an example, in investigating the potential use of HSV-1716 with a marker gene lacZ under the control of the latency-associated transcripts promoter as a gene therapy vector in central nervous system, McMenamin et al. (Gene therapy 5:594-604, 1998) noted that Adult Albino Oxford (AO) rats were extremely susceptible to clinical side effects due to HSV-1716 infection whereas another Piebald Viral Glaxo (PVG) rat strain was free of side effects (column 1, second paragraph, page 595). In the same study, McMenamin et al. further noted that the non-neurovirulent HSV-1716 has a low level of viral replication and spread to distant sites in the brain of treated rats (column 1, first two paragraphs, page 602). They suggested that further modifications in the HSV-1716 are required to limit viral antigen expression prior to its utilization as a gene therapy vector in the brain. In view of this study, the feasibility in deploying any and all mutant HSV having a modified gamma 34.5 gene, including the HSV-1716, in treating non-neuronal cancer (especially metastatic tumor) bearing non-mouse mammal (usually having a compromised immune system) without any adverse clinical side effects would naturally be questioned. In addition, how effective is the delivery of the mutant HSV to inaccessible metastasized tumors in a host

that has a reasonable preexisting immune response to HSV? The specification does not provide sufficient guidance or example to address these aspects.

With respect to the method of treating a non-neuronal cancer in a mammal, although the claim encompasses any and all routes of administering to the mammal an effective amount of mutant HSV having a modified and non-functional gamma 34.5 gene, the specification fails to teach or demonstrate the effectiveness of any other modes of delivery besides direct tumoral injection of the mutant HSV. As already mentioned briefly above, how effective would the treatment be if the mutant HSV is administered into a mammal at distant sites from the tumor, and in the presence of a competent host immune response? Vector targeting (for this instant, the mutant HSV) *in vivo* to desired tissues and organs continues to be unpredictable and inefficient. This is supported by numerous teachings in the art. For example, Deonarain (Exp. Opin. Ther. Patents 8:53-69, 1998) indicated that one of the main obstacles hampering a successful gene therapy is the "ability to target a gene to a significant population of cells and express it at adequate levels for a long enough period of time." (page 53, first paragraph). Deonarain also reviewed new techniques under experimentation in the art which show promises. Verma & Somia (Nature 389:239-242,1997) reviewed various vectors known in the art for use in gene therapy, and the problems which are associated with each. They also indicated clearly that at the time of the claimed invention, resolution to vector targeting had not been achieved in the art (see the entire article). Verma & Somia discussed the role of the immune system in inhibiting the efficient targeting of viral vectors such that an efficient expression is not achieved (see page

239, and second and third columns of page 242). The instant specification fails to teach one of skill in the art how to overcome the unpredictability for *in vivo* vector targeting such that an efficient amount of a mutant HSV can be delivered to primary or metastasized tumors by all modes of delivery.

In regarding to a broad scope of treating any and all non-neuronal cancers in this instant application, the specification fails to provide sufficient evidence demonstrating that cancer cells other than mesothelioma and melanoma cells are susceptible to the oncolytic activity of the mutant HSV of the instant claimed invention in both *in vitro* and *in vivo*. How would one be sure that other non-neuronal cancer cells do not behave similarly as melanoma B16 cells which are resistant to lysis by the mutant HSV of the instant application (Randazzo et al., Virology 211:94-101, 1995)?

With respect to the treatment for any and all mammal, the specification fails to provide sufficient guidance, direction and evidence demonstrating that the therapeutic effect of the HSV mutant in reducing tumor burden and increasing survival in tumor bearing mice could be extrapolated to other non-mouse animal, particularly in human. It should be pointed out that gamma 34.5 HSV mutants designated R3616 and R4009 were incapable of replicating in rat glioma and other rat tumor cells, and thus they are not oncolytic. In contrast, these same HSV mutants replicate competently and possess oncolytic activity in murine and human tumor cells (Andreansky et al., PNAS 93:11313-11318, 1996, see column 2, second paragraph, page 11314). Moreover, how well do the SCID mouse models of human malignant mesothelioma and melanoma described in the instant application predict clinical efficacy of the gamma 34.5 HSV mutants in

human? It is well known in the art that efficacy results in animal models do not necessarily translate into similar success in human.

Accordingly, due to the absence of non-murine working examples, the amount of direction and guidance presented regarding the use of gamma 34.5 HSV mutants other than HSV-1716, the unpredictability of the direct virus therapy due to many variable factors controlling an effective therapy, the unpredictability of vector targeting, and the breadth of the claims, it would have required undue experimentation for one skilled in the art to make and use the broadly claimed invention.

***Written Description***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claim 10 is rejected under 35 U.S.C. 112, first paragraph, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from a written description (e.g. sequenced); or (3) deposited.

The claim is drawn to the mutant herpes simplex virus strain 1716.

It is unclear if mutant virus strain 1716 is known and publicly available, or can be reproducibly isolated without undue experimentation. Clearly, without access to mutant virus strain 1716, it would not be possible to practice the claimed invention. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit

of the above virus, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of the claimed virus is an unpredictable event.

Applicant has not disclosed the deposit of mutant virus strain 1716. If a deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples can not be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications. Applicant's provision of these assurances would obviate this objection/rejection.

Affidavits and declarations, such as those under 37 C.F.R. 1.131 and 37 C.F.R. 1.132, filed during prosecution of the parent application do not automatically become a part of this application. Where it is desired to rely on an earlier filed affidavit, the

applicant should make the remarks of record in the later application and include a copy of the original affidavit filed in the parent application.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of the deposit.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP 1.804 (b).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-10 provide for the use of a mutant herpes simplex virus but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it

merely recites a use without any active, positive steps delimiting how this use is actually practiced.

In claims 1, 2, 11, 12 and dependent claims of claim 1, the phrase "non-neuronal cancer" is unclear. Since the term is not defined in the specification, does it encompass metastasized melanoma in the brain? Or the term encompasses strictly non-neuronal cancers outside the central and peripheral nervous system. Clarification is requested.

In claim 7 and its dependent claim 8, the phrase "a deletion of" is unclear and renders the claims indefinite. Is it a deletion of the BamH1 restriction fragment of the long terminal repeat of the viral genome? If so, please state it as such.

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the mutant herpes simplex virus infects, replicates, and lyses non-neuronal tumor cells, and thereby treating a non-neuronal cancer in a mammal. Otherwise, how would a simple administering step of a mutant herpes simplex virus in a mammal result in treating a non-neuronal cancer as stated in the preamble of the claim? Clarification is requested.

In claim 12, the term "an agent" is unclear and indefinite. Since the term is not defined in the specification, the metes and bound of the claim can not be clearly defined. Clarification is needed.

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the infection,

replication and lysis of non-neuronal cancer cells by the mutant herpes simplex virus of the claimed agent for treating non-neuronal cancer. Clarification is required.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-10 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by MacLean et al. (J. Gen. Virol. 72:631-639, 1991) or Brown et al. (WO 92/13943 with a publication date 8/20/1992).

The claims are drawn to a mutant herpes simplex virus (preferably a herpes simplex virus type I of strain 1716) which has been modified in the gamma 34.5 gene such that the gene is non-functional, and wherein the modification is the deletion of the BamHI restriction fragment of the long terminal repeat of the viral genome from 0.1 to 3kb or from 0.7 to 0.8kb. Claim 12 is directed to an agent for treating a non-neuronal cancer, comprising a mutant herpes simplex virus which has been modified in the gamma 34.5 gene such that the gene is non-functional. The intended uses of these composition claims are not given any patentably weight in view of the prior art.

Both MacLean et al. and Brown et al. disclosed mutant herpes simplex virus type 1 variants (strains 1714 and 1716) having the above required elements (see abstract and Fig. 3, page 634 in MacLean et al.). Thus, the references clearly anticipate the claimed invention.

Claims 1-5, 7-8 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Taha et al. (J. Gen. Virol. 70:705-716, 1989).

The claims are directed to a mutant herpes simplex virus which has been modified in the gamma 34.5 gene such that the gene is non-functional, and wherein the modification is the deletion of the BamHI restriction fragment of the long terminal repeat of the viral genome from 0.1 to 3 kb. Claim 12 is drawn to an agent for treating a non-neuronal cancer, comprising the same mutant herpes simplex virus. For composition claims, their intended uses are not given any patentably weight in view of the prior art.

Taha et al. disclosed a variant of herpes simplex virus type 2 strain HG52 having a 1.5 kb deletion within each copy of BamHI *v* in the long repeat region of the genome (see abstract, last paragraph of page 705). Therefore, the reference clearly anticipates the instant claimed invention.

Claims 1-8 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Chou et al. (Science 250:1262-1266, 1990) or Markert et al. (Neurosurgery 32:597-603, 1993).

The claims are directed to a mutant herpes simplex virus which has been modified in the gamma 34.5 gene such that the gene is non-functional, and wherein the modification is the deletion of the BamHI restriction fragment of the long terminal repeat of the viral genome from 0.1 to 3 kb, and an agent comprising the same mutant herpes simplex virus for treating a non-neuronal cancer. Claim 6 specifically drawn to a type I herpes simplex virus mutant. As stated above, intended uses of composition claims are not given any patentably weight.

Both Chou et al. and Markert et al. disclosed a recombinant herpes simplex virus-1 (R3616) having 1kb deletion of DNA in each copy of the gamma 34.5 gene within the BamH1 restriction fragment of the long terminal repeat of the viral genome (See Fig.1 and column 3, page 1263 and page 1264 in Chou et al.; column 1, third paragraph, page 598 in Markert et al.). Thus, the references anticipate the instant claimed invention.

It should be noted that the same mutant herpes simplex virus-1 or similar mutants containing all elements in the claims are disclosed in Roizman (US Patent No. 5,328,688 with a publishing date 7/12/1994), Martuza et al. (US Patent No. 5,585,096 with a filing date 6/23/1994), Mineta et al. (Nat. Med. 1:938-943, 1995), and Martuza et al. (US Patent No. 5,728,379 with a filing date 6/7/1995).

Claims 1-12 are rejected under 35 U.S.C. 102(a) as being anticipated by Ranazzo et al. (Virology 211:94-101, 1995).

Claims 1-10 and 12 are drawn to a mutant herpes simplex virus which has been modified in the gamma 34.5 gene such that the gene is non-functional and an agent

comprising the same mutant herpes simplex virus. Claim 11 is directed to a method of treating a non-neuronal cancer in a mammal, which method comprises the administering an effective amount of the same mutant herpes simplex virus into the mammal.

Randazzo et al. disclosed a method using an HSV-1 mutant 1716 having a 759-bp deletion in gamma 34.5 gene to treat murine melanoma (derived from injected Harding-Passey melanoma cells) developed intracranially in C57Bl/6 mice. Stereotactic injection of the neuroattenuated HSV-1 strain 1716 into intracranial melanoma bearing mice resulted in complete tumor regression and the long-term survival for some of the treated animals (See abstract, Fig. 2 on page 97). Therefore, the reference clearly anticipates the claimed invention.

Claim 11 is provisionally rejected under 35 U.S.C. 102(e) as being anticipated by copending Application No. 08/776350 which has a common inventor with the instant application.

Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. 102(e), if patented. This provisional rejection under 35 U.S.C. 102(e) is based upon a presumption of future patenting of the copending application.

Applicant's claimed invention is drawn to a method of treating a non-neuronal cancer in a mammal comprising the step of administering to the mammal an effective

amount of a mutant herpes simplex virus which has been modified in the gamma 34.5 gene such that the gene is non-functional.

The copending Application No. 08/776350 disclosed a method of treating murine melanoma developed intracranially in mice by the administration to the tumor bearing mice an effective dose of neuroattenuated HSV-1 strain 1716 having a non-functional gamma 34.5 gene (See example 3). Thus, the copending Application with an earlier filing date anticipates the applicant's claimed invention.

This provisional rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

This rejection may not be overcome by the filing of a terminal disclaimer. See *In re Bartfeld*, 925 F.2d 1450, 17 USPQ2d 1885 (Fed. Cir. 1991).

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 11 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 43-58 of copending Application No. 08776350. Although the conflicting claims are not identical, they are not patentably distinct from each other because a method of treating a non-neuronal cancer in a mammal comprising the administering into said mammal an effective amount of a mutant herpes simplex virus which has been modified in the gamma 34.5 gene such that the gene is non-functional of the instant application reads on a method of treating a metastatic tumor occurring in but not originating from the central nervous system of a human, and a method of treating a melanoma cancer in a human using an effective amount of a mutant herpes simplex virus type I which has a non-functional gamma 34.5 gene in the long repeat region (RL) of the copending Application. The scope of claim 11 in the instant application is broader than those of the copending Application because non-neuronal cancer in a mammal encompasses metastatic and melanoma in human, and a mutant herpes simplex virus having a non-functional gamma 34.5 encompasses a herpes simplex virus type I with the same mutation.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Conclusions***

**No claim is allowed.**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (703) 308-8339.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda, J.D., may be reached at (703) 305-6608.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-2801.

**To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1632.**

Papers related to this application may be submitted to Group 160 by facsimile transmission. Papers should be faxed to Group 160 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The CM1 Fax Center number is or (703) 305-3014 or (703) 308-4242.

Karen M. Hauda

KAREN HAUDA
PRIMARY EXAMINER